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Review Article

Environmental exposure to organophosphorus nerve agents

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ABSTRACT

Exposure to organophosphorus nerve agents, the most deadly chemical warfare agents, is possible in a variety of situations, such as destruction of chemical warfare agents, terrorist attacks, armed conflicts or accidents in research laboratories and storage facilities. Hundreds of thousands of tons of chemical munitions were disposed of at the sea in the post World War II period, with European, Russian, Japanese and US coasts being the most affected. Sulfur mustard, Lewisite and nerve agents appear to be the most frequently chemical warfare agents disposed of at the sea. Addressing the overall environmental risk, it has been one of the priorities of the world community since that time. Aside from confirming exposure to nerve agents in the alleged use for forensic purposes, the detection and identification of biological markers of exposure are also needed for the diagnosis and treatment of poisoning, in addition to occupational health monitoring for specific profiles of workers. When estimating detrimental effects of acute or potential chronic sub-lethal doses of organophosphorus nerve agents, released accidentally or intentionally into the environment, it is necessary to understand the wide spectra of physical, chemical and toxicological properties of these agents, and predict their ultimate fate in environmental systems.

1. Introduction

Bearing in mind that over 100 dumping sites in the Baltic region (Gotland Deep, Bornholm Deep, Little Belt, Skagerrak Strait) were used for depositing chemical warfare agents (CWAs) between 1945 and 1970, as well as over 60 sites in the Gulf of Mexico, the coasts of Japan and the oceans on both coasts of the USA – which has been confirmed in the CWA exposure reports by hundreds of fishermen who have caught dangerous cargo via their nets – this method of exposure is not to be underestimated. Moreover, at several places all over the world, e.g. in the US, China, and Europe, old chemical munition has been lost or buried and could be accidently released as it is shown in Fig. 1 (CHEMSEA, 2013; Vučinić et al., 2014).

While a wide variety of chemical warfare agents including also sulfur mustard, Lewisite, have been dumped or buried, this manuscript deals with problems that arise from nerve agents exposure. The aim of this review is to raise the attention of environmental exposure to NAs that could persist in different media long after initial exposure, producing a wide range of toxic effects. Better understanding of the time frame for detection of biological markers of exposure to NAs is critical for diagnosis and treatment in uncertain cases of exposure.

After the first confirmed use of nerve agents (NAs) in the Iran-Iraq War (1980–1988), when the Iraqi army used tabun and sarin against the Iranian forces (Majnoon Island) and the civilian population

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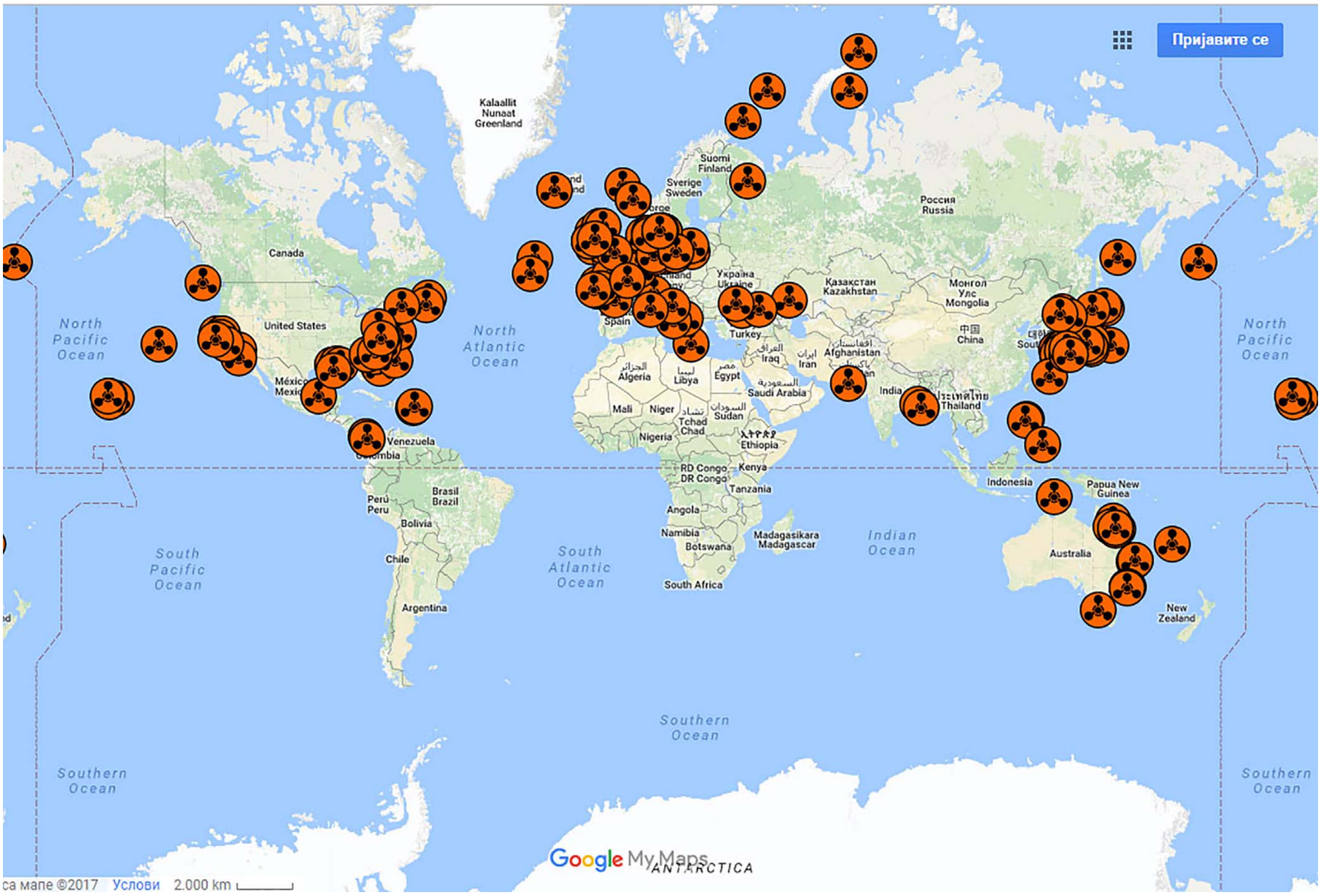

Fig. 1. Chemical Weapon Munitions Dumped at Sea – Available at: www.nonproliferation.org/chemical-weapon-munitions-dumped-at-sea, August 1, 2017.

(Halabjah) (Balali-Mood and Balali-Mood, 2008), these deadly agents were used for the terrorist attacks in Japan. The terrorist attacks in Matsumoto in 1994, which claimed the lives of 7 people (Nakajima et al., 1999) and Tokyo in 1995, with over 5500 injured and 13 dead (Nagao et al., 1997; Murata et al., 1997), showed the necessity for development of specific diagnostic methodology for identifying nerve agents, which had not existed until then (Salem et al., 2008a,b).

The importance of the engagement of the Organisation for the Prohibition of Chemical Weapons (OPCW) and the chain-of-custody procedures had became obvious after the UN mission in the Syrian Arab Republic, performed by the OPCW and WHO teams which had investigated the Ghouta and other sites of attacks. Difficulties in establishing a credible epidemiological pattern through interviews with first responders, victims and medical personnel had confirmed the importance of designated laboratories (Pita and Domingo, 2014).

The core objective of the OPCW is the promotion and adherence to the Chemical Weapons Convention (CWC). Among other activities, the OPCW performs inspections of facilities for destroying CWAs, industry inspections, challenge inspections and investigations of alleged use, in order to verify destruction and non-proliferation of chemical agents. The OPCW technical secretary provides off-site analysis through a network of designated laboratories proficient in NAs analysis and their degradation products at concentrations greater than 1 ppm in environmental and man-made samples (OPCW, 1994; Black and Read, 2013). Since 2016 the OPCW has had 17 designated laboratories for analysis of biological samples. Some of them were already involved in the verification of poisoning induced by CWAs during the recent events in Syria.

Aside from confirming exposure to NAs in the alleged use for forensic purposes, the detection and identification of biological markers of exposure is also needed for the diagnosis and therapy of intentional or accidental poisoning, in addition to occupational health monitoring for specific worker profiles (Black and Read, 2013).

2. Nerve agents and toxicity

Chemical weapons, including OP NAs, have been used for decades in armed conflicts and terrorist attacks, but accidental leakage from industrial and storage facilities, laboratories, dumping and chemical weapon incineration sites, has also led to health issues and even deaths in those exposed. Although the scientific literature on the NAs is extensive (PubMed search listed 54.400 articles), less than 10% of articles deal with the environmental exposure to OP Nas (Vučinić et al., 2014; Davisson et al., 2005; Kingery and Allen, 1995; Lionetto, 2013; USACHPPM/ORNL, 1999).

Published articles refer mainly to the significant alterations in ecosystems with CWA dumpsites, where the solubility and hydrolysis rates of CWAs' innate toxicity had been assessed for marine environment risk prediction. There is indeed evidence of chronic toxicity, though studies in marine organisms have not exhibited concerning amount in tissues of these agents and their by-products. Acute exposure to an agent presents the major human health risk, either by accidental recovery of a CWA on a fishing vessel or by munitions washed ashore onto beaches (CHEMSEA, 2013).

In order to provide successful medical protection it is essential to understand the toxicity of NAs (VX vapor is the most toxic with LCt_{50} of 10 $mg/min/m^3$, and tabun is the least toxic with LCt_{50} of 400 $mg/min/m^3$), but also the relevant physicochemical properties of NAs such as: volatility (for sarin 22,000 mg/m^3 and VX 10.5 mg/m^3), vapor pressure showing how quickly an NA will evaporate (for sarin at 20 °C

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